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Pericardial Disease

Changes in QRS Voltage in Cardiac Tamponade and Pericardial Effusion: Reversibility After Pericardiocentesis and After Anti-Inflammatory Drug Treatment

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OBJECTIVES The goal of this study was to define the association between low QRS voltage and cardiac tamponade or pericardial effusion and to assess the reversibility of low QRS voltage after therapeutic procedures.

BACKGROUND It is unclear whether low QRS voltage is a sign of cardiac tamponade or whether it is a sign of pericardial effusion per se.

METHODS In a prospective study design, we recorded consecutive 12-lead electrocardiograms and echocardiograms in 43 patients who were referred to our institution for evaluation and therapy of a significant pericardial effusion. Cardiac tamponade was present in 23 patients (53%). Low QRS voltage (defined as maximum QRS amplitude <0.5 mV in the limb leads) was found in 14 of these 23 subjects (61%). Nine of these 14 patients were treated by pericardiocentesis (group A). Five patients received anti-inflammatory medication (group B). Group C consisted of nine patients with pericarditis and significant pericardial effusion who had no clinical evidence of tamponade.

RESULTS In group A, low QRS voltage remained largely unchanged immediately after successful pericardiocentesis (0.36 ± 0.17 mV before vs. 0.42 ± 0.21 mV after, p = NS), but QRS amplitude recovered within a week (0.78 ± 0.33 mV, p < 0.001). In group B, the maximum QRS amplitude increased from 0.40 ± 0.20 mV to 0.80 ± 0.36 mV (p < 0.001) within six days. In group C, all patients had a normal QRS amplitude initially (1.09 ± 0.55 mV) and during a seven-day follow-up (1.10 ± 0.56 mV, p = NS).

CONCLUSIONS Low QRS voltage is a feature of cardiac tamponade but not of pericardial effusion per se. Our findings indicate that the presence and severity of cardiac tamponade, in addition to inflammatory mechanisms, may contribute to the development of low QRS voltage in patients with large pericardial effusions. (J Am Coll Cardiol 2001;38:219–26) © 2001 by the American College of Cardiology

Cardiac tamponade and pericardial effusion have long been associated with low voltage of the 12-lead electrocardiogram (ECG) (1,2), and the diagnostic accuracy, sensitivity and specificity of this ECG finding have previously been reported (3,4). However, the question of whether low QRS voltage is a sign of cardiac tamponade or of pericardial effusion, per se, has not been specifically addressed. Various animal models have been used to study electrocardiographic features during intrapericardial fluid injection (5–7). However, in these experimental approaches, the authors focused on the impact of acute cardiac tamponade, whereas gradual intrapericardial fluid accumulation without tamponade was not examined.

Different mechanisms have been proposed to explain low QRS voltage associated with pericardial effusion and cardiac tamponade. These mechanisms include mechanicoelectrical alterations of the myocardium, distance of the heart from body surface electrodes and reduction of cardiac size and volume (5–7). However, the influence of different therapeutic interventions such as pericardiocentesis or anti-inflammatory drug treatment on reduced QRS voltage has not been elucidated. This investigation was designed to clarify the association between low QRS voltage and cardiac tamponade or pericardial effusion and to assess the reversibility of low QRS voltage after different therapeutic interventions.

METHODS

In a prospective design, consecutive 12-lead ECGs and echocardiograms were recorded in 43 hospitalized patients (age 56 ± 18 years, 27 men/16 women) who were referred to our institution (University Clinic Essen) for evaluation and management of a significant pericardial effusion (volume of the effusion >300 ml, mean 460 ml ± 180 ml). Patients were referred from a variety of medical and surgical services, including cardiothoracic surgery. The causes of the effusion were previous cardiothoracic surgery (n = 19),

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Abbreviations and Acronyms
CI = confidence interval
ECG = electrocardiogram
LV = left ventricle or left ventricular

cancer (n = 13), heart failure (n = 3), tuberculosis (n = 1), renal failure (n = 3), postmyocardial infarction (n = 1) and idiopathic (n = 3).

Clinical features of cardiac tamponade were present in 23 of these 43 patients (53%). Signs and symptoms included right ventricular compression (n = 19), right atrial compression (n = 12), dyspnea at rest (n = 17), neck vein distension (n = 10) and inferior vena cava plethora (n = 9), indicating the need for therapy in all patients.

Low QRS voltage (defined as maximum QRS amplitude <0.5 mV in the limb leads, mean 0.39 mV ± 0.22 mV) was observed in 14 of 23 subjects with cardiac tamponade (61%). Nine of these 14 patients (seven men, two women, age 51 ± 14 years, group A) were treated by pericardiocentesis guided by two-dimensional echocardiography (8). In five patients (two men/three women, 48 ± 18 years, group B), anti-inflammatory medication was started (duration 4 to 21 days, mean 7 ± 7 days). Medical treatment was chosen due to Dressler syndrome (n = 2), severe thrombocytopenia (n = 1), oral anticoagulation (n = 1) or recurrent effusion (n = 1). In this group, two patients had a history of gastrointestinal ulcer disease. Treatment was performed either with prednisolone in tapering dosage starting with 500 mg (n = 1) or 100 mg (n = 1) or nonsteroidal anti-inflammatory agents (diclofenac 3 × 50 mg/day [n = 2], indomethacine 50 mg/day [n = 1]). Group C consisted of nine patients (six men/three women, age 42 years ± 18 years) with pericarditis and significant pericardial effusion (mean volume 472 ml ± 272 ml) but no clinical evidence of tamponade.

In all study subjects, a baseline 12-lead ECG was recorded. In group A, all patients received consecutive ECG recordings for one week after pericardiocentesis. In group B, a second ECG was obtained 6 days ± 3 days after initiation of anti-inflammatory drug treatment. In group C, a second ECG was obtained after 7 days ± 2 days during follow-up. In all patients, the volume of the pericardial effusion was quantified by two-dimensional echocardiography every 48 or 72 h.

12-lead ECG. An electrocardiograph (Marquette, Hellige; Freiburg, Germany) was used to record all 12-lead ECGs. Paper speed was 50 mm/s, and standardization was 10 mV/10 mm. Each ECG was independently reviewed by an experienced cardiologist who had no knowledge of the patients' clinical history or echocardiographic results.

Echocardiography. Images were recorded with patients in the left lateral decubitus position with a 3.75-MHz sector probe using a Toshiba SSA 380 A Power Vision or a Hewlett Packard Sonos 1500 machine (both commercially available). The echocardiographic examination was done using standard views and techniques according to the guidelines of the American Society of Echocardiography (9). The volume of the pericardial effusion was quantified as previously described by Horowitz and co-workers (10).

Table 1. Clinical Data

	Group A (n = 9)	Group B (n = 5)	Group C (n = 9)
Age (yr)	51 ± 14	46 ± 16	42 ± 18†
Gender, M/F	7/2	2/3	6/3
BSA (m^2)	1.99 ± 0.30	1.90 ± 0.48	1.93 ± 0.45
Heart rate (beats/min)	94 ± 15	92 ± 16	88 ± 24
LVDDI (cm/m^2)	2.3 ± 0.3	2.4 ± 0.4	2.5 ± 0.4
LVSDI (cm/m^2)	1.4 ± 0.4	1.5 ± 0.5	1.6 ± 0.4
IVS (cm)	1.0 ± 0.4	1.2 ± 0.4	1.1 ± 0.4
PW (cm)	1.0 ± 0.3	1.0 ± 0.2	1.1 ± 0.3
LVMMI (g/m^2)	124 ± 37	141 ± 47	142 ± 60
LVEDVI (ml/m^2)	56 ± 18	55 ± 22	54 ± 12
LVESVI (ml/m^2)	28 ± 11	25 ± 14	25 ± 8
SVI (ml/m^2)	28 ± 18	30 ± 13	29 ± 11
SBP (mm Hg)	114 ± 24	112 ± 31	134 ± 26*
DBP (mm Hg)	78 ± 10	75 ± 18	82 ± 16
EF (%)	46 ± 9*	54 ± 9	55 ± 8

*p < 0.05 compared with each of the other groups; †p < 0.05 compared with group A.
BSA = body surface area; DBP = diastolic blood pressure; EF = ejection fraction; IVS = thickness of the interventricular septum; LVDDI = left ventricular diastolic diameter index; LVEDVI = left ventricular end-diastolic volume index; LVESVI = left ventricular end-systolic volume index; LVMMI = left ventricular muscle mass index; LVSDI = left ventricular systolic diameter index; PW = thickness of the posterior wall; SBP = systolic blood pressure; SVI = left ventricular stroke volume index.

Statistics. Data are expressed as mean value ± SD. Variables derived from echocardiography and ECG analysis were compared between the distinct groups using one-way analysis of variance (ANOVA) and post-hoc Bonferroni analysis. For variables with a non-normal distribution, a one-way ANOVA on ranks was employed. A difference was considered significant at $p < 0.05$.

RESULTS

Clinical data and baseline echocardiographic findings. Patient demographics are given in Table 1. No differences between the three study groups were observed with respect to heart rate, left ventricular (LV) diameter and LV volume indexes, interventricular septum and posterior wall thickness and LV muscle mass index. The systolic blood pressure was reduced in group A and group B. Left ventricular ejection fraction was lower in group A patients than it was in group B and C patients.

Volume measurements. In group A, the pericardial effusion was successfully drained by pericardiocentesis in all patients (572 ml ± 245 ml vs. 55 ml ± 32 ml, $p < 0.001$). None of the patients had a recurrent effusion at a six-day follow-up (55 ml ± 32 ml vs. 64 ml ± 38 ml, p = NS). In group B, the volume of the effusion significantly decreased from 461 ml ± 184 ml to 141 ml ± 82 ml ($p < 0.001$) at day 6 after initiation of anti-inflammatory drug treatment. In group C, the volume of the pericardial effusion did not change significantly during a seven-day follow-up (472 ml ± 272 ml vs. 390 ml ± 233 ml, p = 0.06). At the baseline

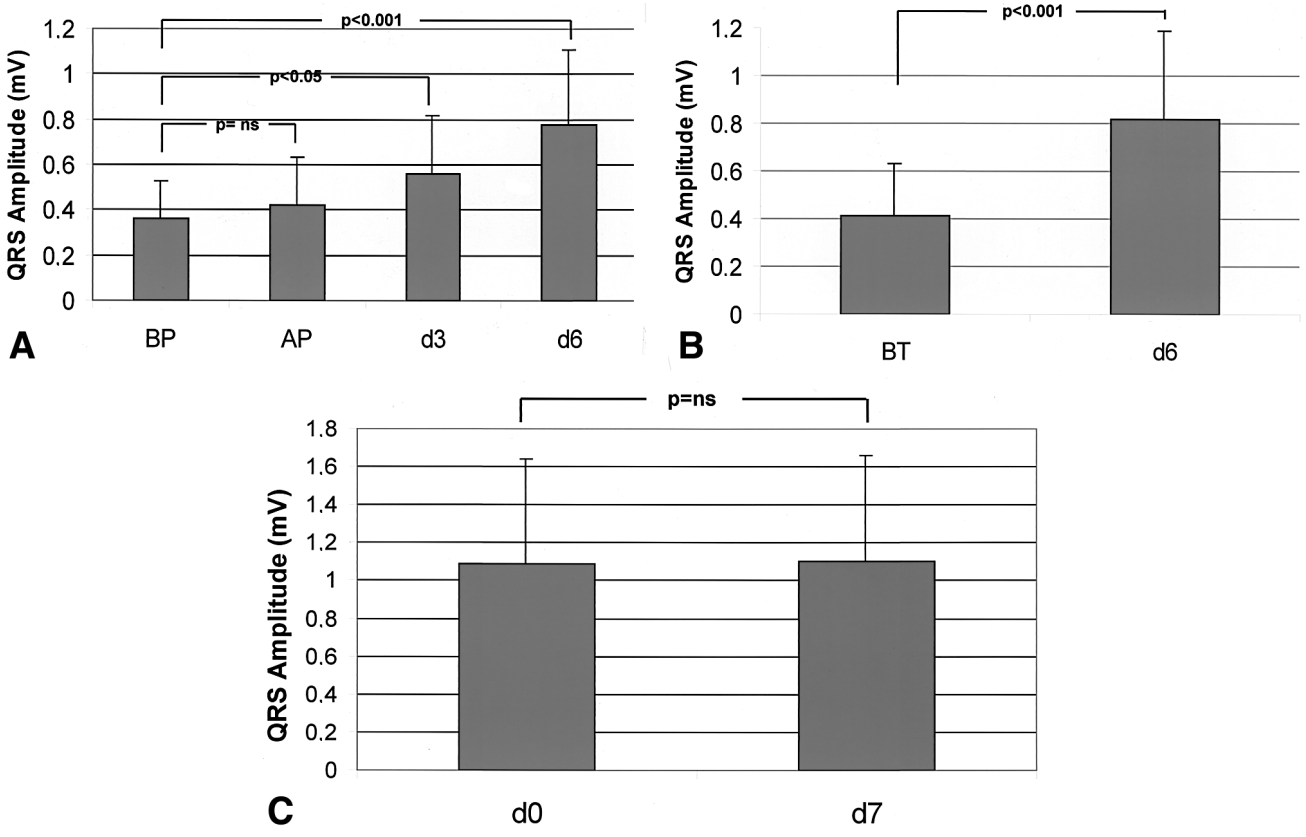

Figure 1. **(A)** Maximum QRS amplitude in the limb leads in group A patients, who where treated with pericardiocentesis. AP = immediately after pericardiocentesis; BP = before pericardiocentesis; d3 = three days after pericardiocentesis; d6 = six days after pericardiocentesis. **(B)** Maximum QRS amplitude in the limb leads in group B patients, who were treated with anti-inflammatory medication. BT = before anti-inflammatory treatment; d6 = six days after initiation of anti-inflammatory medication. **(C)** Maximum QRS amplitude in the limb leads in group C patients (pericarditis). d0 = baseline measurement; d7 = after a seven-day follow-up.

echocardiographic examination, the volume of the effusion was smaller in groups B and C than in group A ($p < 0.05$, respectively). At follow-up, a larger volume of the pericardial effusion remained in group C patients in comparison with groups A and B ($p < 0.01$, respectively).

ECG signs. In group A, the maximum QRS voltage in the limb leads remained nearly unchanged immediately after pericardiocentesis but consecutively increased within six days (Fig. 1A). In group B, maximum QRS amplitude significantly increased six days after initiation of anti-inflammatory treatment (Fig. 1B). In group C, the baseline ECG showed a normal maximum QRS amplitude in all patients, which remained nearly unchanged during follow-up (Fig. 1C).

At the baseline examination, comparison between groups showed a significant reduction of the QRS amplitude in groups A and B in comparison with group C (0.36 mV ± 0.17 mV and 0.40 mV ± 0.20 mV vs. 1.09 mV ± 0.55 mV, $p < 0.001$, respectively). The difference between group A and group B was not statistically significant. The maximum QRS amplitude after anti-inflammatory therapy was significantly higher in group B patients than in group A patients immediately and three days after pericardiocentesis (0.82 mV ± 0.37 mV vs. 0.42 mV ± 0.21 mV, $p < 0.001$ and 0.82 mV ± 0.37 mV vs. 0.56 mV ± 0.26 mV, $p < 0.01$, respectively). Six days after initiation of therapy, no significant difference in QRS amplitude was detected between groups A and B (0.78 ± 0.33 vs. 0.82 ± 0.37, p = NS). At this time, QRS amplitude remained significantly decreased in groups A and B in comparison with group C (0.78 ± 0.33 and 0.82 ± 0.37 vs. 1.10 ± 0.56, $p < 0.05$, respectively).

Representative examples of groups A and B with simultaneous ECG and echocardiography recordings before and after treatment are shown in Figure 2A to C and Figure 3A and B.

DISCUSSION

In the current investigation, we report for the first time serial, simultaneous ECG and echocardiographic recordings in patients with large pericardial effusions. The main finding is that low QRS voltage was present in the majority of subjects with cardiac tamponade but not in patients with pericarditis and large pericardial effusions who were clinically stable. Low QRS voltage persisted immediately after successful pericardiocentesis, but QRS amplitude recovered within one week (Fig. 1A, Fig. 2A to C). During successful

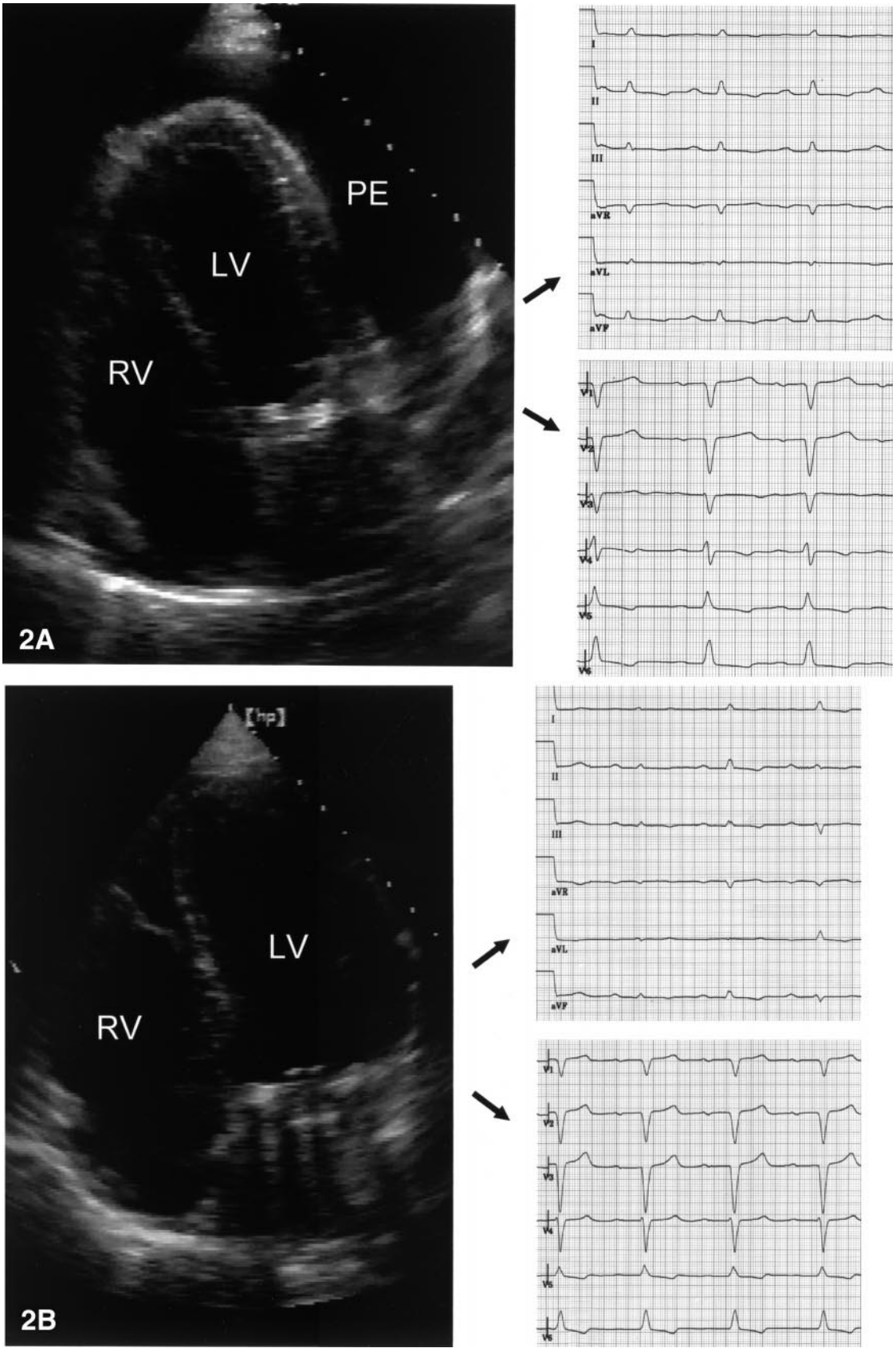

Figure 2. **(A)** Simultaneous echocardiography (**left side of the panel,** apical four-chamber view) and electrocardiogram recordings **(right side of the panel)** in a 64-year-old man who developed significant pericardial effusion (PE) with signs of cardiac tamponade three weeks after mitral valve replacement. Note the reduction of the QRS amplitude in the limb leads and concomitant nonspecific T wave abnormalities. **(B)** Same patient as in **(A)** after successful pericardiocentesis with removal of 600 ml of pericardial fluid. Note the even lower QRS voltage in the limb leads than before pericardiocentesis and the persistence of nonspecific T wave abnormalities. *Figure 2 continued on next page.*

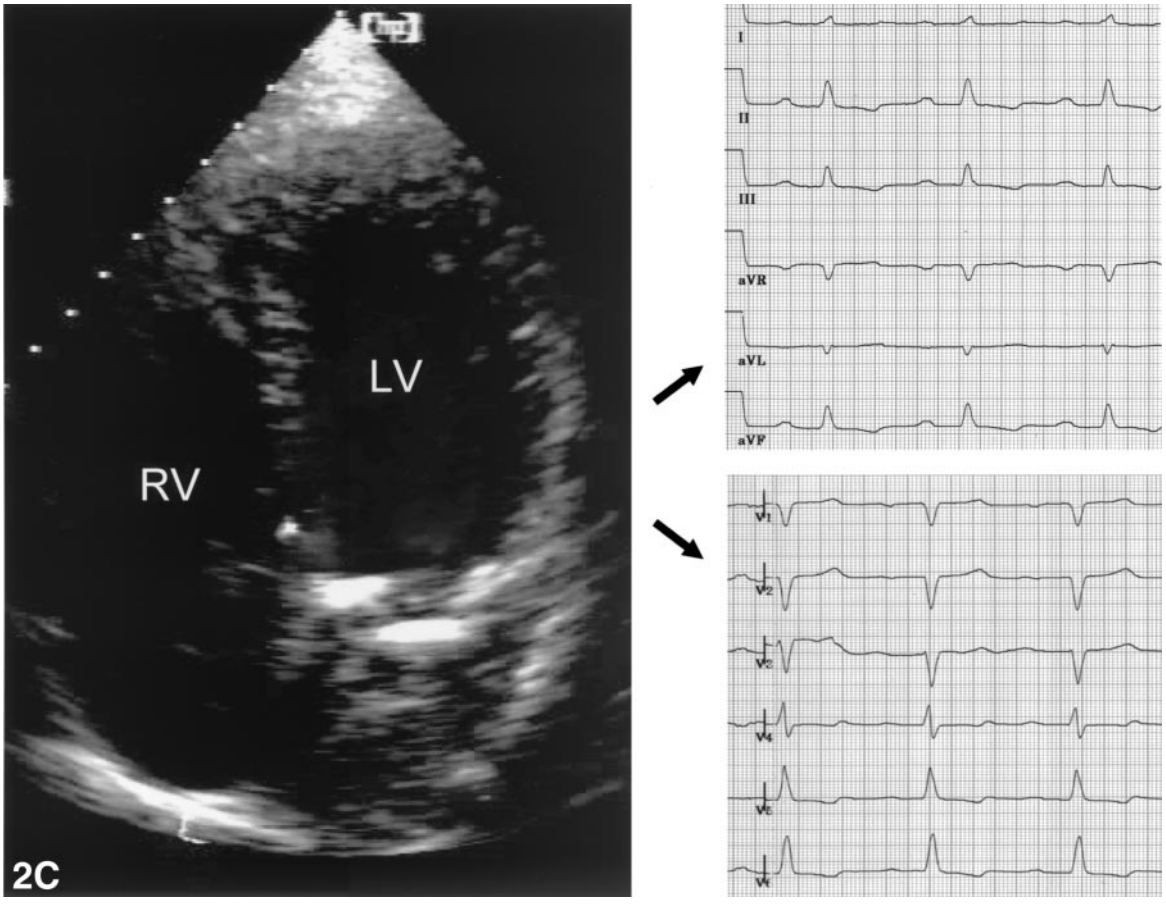

Figure 2. Continued from previous page. (C) Same patient six days after pericardiocentesis. The echocardiogram shows no evidence of recurrent effusion. QRS amplitude in the limb leads significantly increased. LV = left ventricle; RV = right ventricle.

anti-inflammatory treatment, low QRS voltage disappeared within six days (Fig. 1B and Fig. 3A and B). In patients with pericarditis who had a normal QRS amplitude, no change in the QRS amplitude was observed during follow-up (Fig. 1C).

Mechanism of low QRS voltage in pericardial effusion. Several mechanisms have been proposed to explain the association between pericardial effusion and low QRS voltage, namely internal short circuiting of the electrical currents by the accumulated fluid within the pericardial space (6), change in the position of the heart (6), increasing distance from the current generator to the recording electrodes (5,11), decrease in cardiac chamber size and volume (7,12) and changes in the generation and propagation of electrical currents in the myocardium (7). However, only a few investigators have tried to clarify the mechanisms of low QRS voltage with pericardial effusion in an experimental approach (7,11,13).

Karatay and co-workers (7) produced cardiac tamponade in closed-chest pigs by the introduction of saline, blood and plasma into the pericardial space (7). As a consequence, mean limb and precordial lead QRS voltage fell significantly, with no significant difference among these fluids. Electrocardiographic recordings from a unipolar electrode catheter in the right ventricle showed an increase in R wave voltage, whereas body surface recordings of stimuli introduced into the right atrium via a bipolar electrode catheter showed no amplitude change. The authors of this study attributed their results to a reduction of cardiac volume and size during cardiac tamponade. In their view, the results confirmed Brody's hypothesis, which claims that alterations in end-diastolic blood volume will change the magnitude of cardiac electrical potentials recorded at the body surface (12).

In an earlier experiment, Friedman and co-workers (13) studied the electrocardiographic features of experimental cardiac tamponade in closed-chest dogs. In their study, acute cardiac tamponade produced by rapid saline infusion into the pericardium induced reduction of the QRS amplitude and left-axis deviation of the QRS complex, whereas the amplitude of the P wave remained essentially unchanged. Interestingly, in agreement with the findings of Karatay and co-workers, the amplitude of bipolar ventricular ECG increased during tamponade, further supporting Brody's concepts. However, the authors of these animal studies focused on the impact of a rapidly produced cardiac tamponade but not on a gradual intrapericardial fluid accumulation, which more closely reflects the situation in a daily clinical setting.

The findings obtained in our study suggest that different mechanisms may interplay to explain low QRS voltage in patients with pericardial effusion and cardiac tamponade.

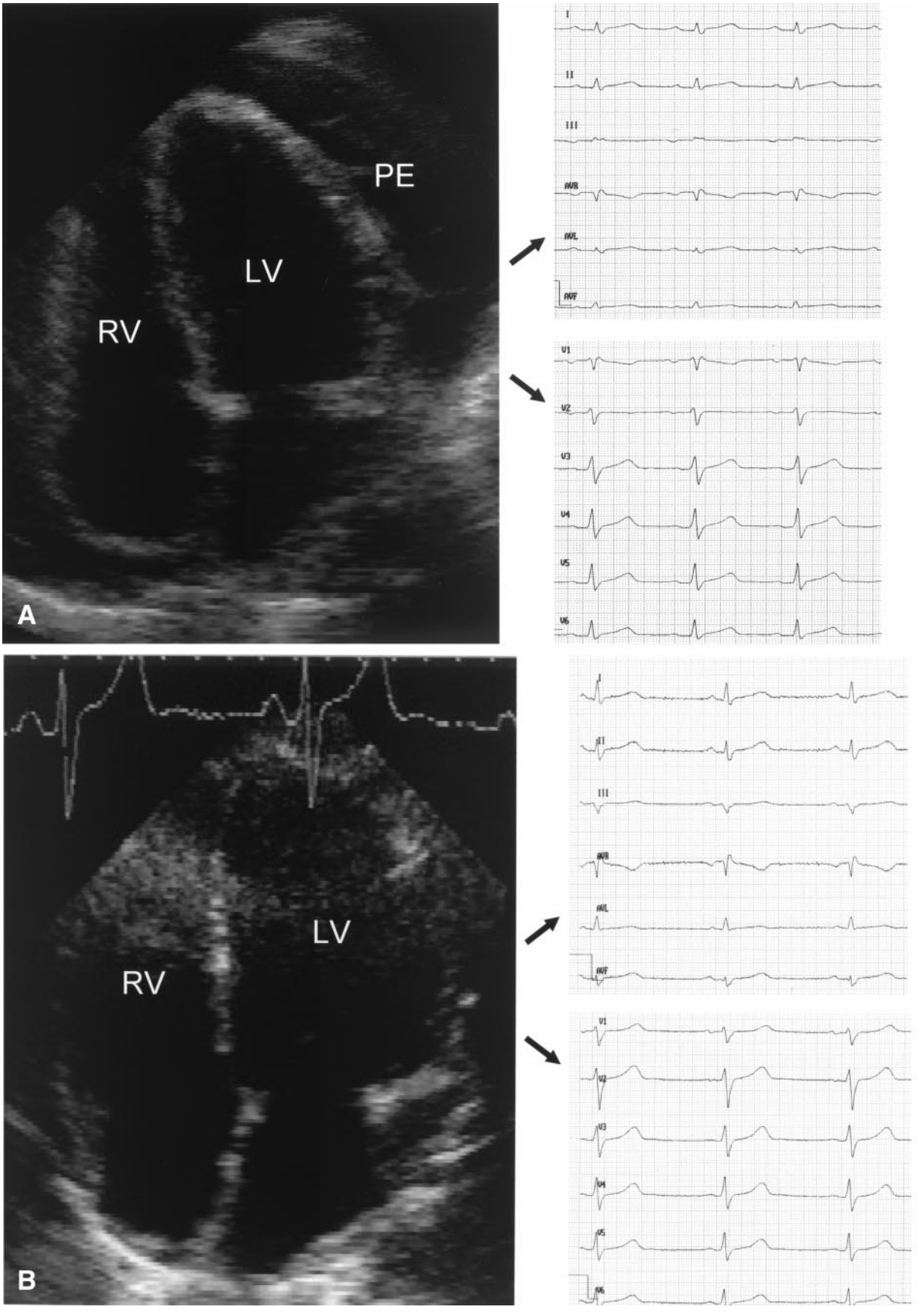

Figure 3. **(A)** A 23-year-old man with acute lymphatic leukemia who was treated with prednisolone due to recurrent malignant pericardial effusion. Note low QRS voltage in the limb leads before initiation of medical treatment. **(B)** Same patient as in **(A)** six days after initiation of anti-inflammatory treatment. Note the change of the QRS axis and the significant increase of maximum QRS amplitude in the limb leads. LV = left ventricle; RV = right ventricle.

The presence and severity of cardiac tamponade seem to be crucial factors because low QRS amplitude was observed only in subjects with clinical evidence of tamponade but not in patients with pericarditis and large effusions who were clinically stable. However, in patients with cardiac tamponade, no changes in the maximum QRS amplitude were observed immediately after pericardiocentesis. Following Brody's hypothesis, successful removal of intrapericardial fluid during pericardiocentesis should have increased the end-diastolic blood volume. Thus, the QRS amplitude should have increased after the procedure.

Other mechanisms that may contribute to the development of low QRS voltage include inflammation as well as changes in the propagation and generation of electrical currents in the myocardium. Previously, it has been demonstrated that the epicardial circumference shortens proportionally less than the endocardial circumference, resulting in different tension distributions (14). Schlant and Hurst (15) have shown the strong impact of these electrical inhomogeneities on the surface ECG. Friedman and co-workers (13) have demonstrated that both intrapericardial and end-diastolic intraventricular pressures rise during cardiac tamponade, leading to compression of the myocardium in between. This increase of end-diastolic ventricular pressure contributes to the approximation of the surfaces of the myocardium. As a consequence, the mechanicoelectrical conditions of the endocardial and the epicardial myocardium become more alike, offering an explanation for the changes present in the surface ECG (7). However, in our study, QRS amplitude normalized six days after initiation of anti-inflammatory treatment, also suggesting a potential role of inflammation.

Low QRS voltage in the management of patients with pericardial effusion. The diagnostic value of low QRS voltage for the diagnosis of pericardial effusion and cardiac tamponade has previously been reported (1,2,4). Eisenberg and co-workers (4) studied ECGs in 107 patients with small effusions, in 29 patients with large and moderate effusions and in 12 patients with cardiac tamponade. They found a mild association of low QRS voltage with large and moderate effusions (odds ratio = 2.5, 95% confidence interval [CI]: 0.9 to 6.5, $p = 0.06$) and a moderate association with cardiac tamponade (odds ratio 4.7; 95% CI: 1.1 to 21.1, $p = 0.004$). In this study, low QRS voltage was only suggestive, but not diagnostic, of cardiac tamponade (4). These findings are in agreement with our observations. In our study population, low QRS voltage was present in 14 of 23 subjects with clinical evidence of tamponade but not in subjects with pericarditis and large effusions. As a consequence, although low QRS voltage is indicative of cardiac tamponade, its absence does not rule out tamponade.

Other investigators studied ECG changes during follow-up in patients with confirmed pericardial effusion or cardiac tamponade. Unverferth and colleagues (16) reported that, in 22 patients after pericardiocentesis, frontal-plane and precordial voltages increased only slightly. In our study, we also observed no significant change of the maximum QRS amplitude immediately or in the first two days after successful pericardiocentesis. Echocardiographic follow-up in our study indicated that this persistent low QRS voltage should not be mistaken as a sign of recurrent effusion in the first days after pericardiocentesis. However, in this study population, QRS amplitude had significantly increased within six days from pericardiocentesis. Thus, in patients who had already shown an increase of the QRS amplitude, another decrease might indicate recurrent pericardial effusion, but this remains speculative.

Study limitations. Several limitations of our study should be noted. First, only patients with large pericardial effusions (>300 ml) were included. Because the first ECG was obtained simultaneously with the first echocardiogram, it cannot be excluded that some patients had pre-existing low QRS voltage. Second, no attempt was made to differentiate between patients with acute and chronic pericardial effusion. Accordingly, results of a cytological and chemical analysis of the pericardial fluid were not considered. Third, no attempt was made to measure intrapericardial or central venous pressures at the time of pericardiocentesis. Such measurements might have added valuable information with respect to the ECG changes observed in subjects with cardiac tamponade. Finally, our study group was small, and the results should be confirmed in a larger patient population.

Conclusions. Low QRS voltage is observed in the majority of subjects with cardiac tamponade but not in patients with pericarditis and large pericardial effusions. After pericardiocentesis and after initiation of anti-inflammatory treatment, QRS amplitude normalizes within one week. Our findings suggest that the presence and severity of cardiac tamponade, but also inflammatory mechanisms, may contribute to the development of low QRS voltage in patients with pericardial effusion.

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